

REMARKS/ARGUMENTS

Reconsideration of the above-identified application respectfully requested.

1. Amendments to the Claims and Specification.

Amendment of page 1 of the specification was requested by the Examiner to properly claim priority to parent applications. The Examiner newly objects to the inclusion of the phrase "said applications are herein incorporated by reference." Although this language was entered into the specification over three years ago by the same Examiner, in an attempt to materially advance prosecution Applicants yield to the advice of the Examiner. Therefore such language has been deleted.

Claims 29-35 were rejected as indefinite in the recitation of "enriched" because the examiner finds that the meaning of "enriched" is unclear, is not defined and has no art recognized meaning. Claims 29-35 were previously amended to replace the term "helper cell" with the accepted art term "T helper cell". This amendment was made at the suggestion of the Examiner and Applicants made such amendment to the claims seeking to particularly point out the subject matter of the invention in a manner acceptable to the Examiner. Said amended claim language has now been rejected as indefinite. Applicants do not agree, as "enriched T helper cell population" has an accepted meaning in the art, with such meaning understood previously by the Examiner. A dictionary definition of enrich is "to give greater value or importance to." See Webster's New World Dictionary. The meaning of "enriched T helper cell population" is supported in the specification, and recognized in the art as meaning a T helper cell population that has been given greater value or importance than the unexpanded or unstimulated helper T cell population.

While the Applicants preference is to forgo further amendments to the claims, and believe that it is unnecessary to amend the claim language in order to meet the requirements of 35 USC §112, Applicants nonetheless submit claim amendments to all claims substituting the word "expanded" for the word "enriched." Applicants submit this amendment solely in an attempt to satisfy the Examiner and such amendments are merely for ministerial purposes. Variations of the verb "expand" are utilized throughout the application, in particular in the Summary of the Invention at page 4, line 32 and page 5, line 12. If such amendments do not meet with the Examiner's approval, Applicants invite the Examiner to telephone the Applicants' attorney to discuss language that is acceptable to the Examiner.

No new matter is added by virtue of these claim amendments. Moreover, such claim amendments are for clarification purposes by defining claim terms with alternative expressions and definitions. Importantly, Applicants assert that no claims have been narrowed with the meaning of *Festo* (*Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 US 722, 112 S.Ct. 1831, 152 L.Ed.2d 944, 62 USPQ2d 1705 (2002)). See also *Interactive Pictures Corp. v. Infinite Pictures Inc.*, Fed Cir., No. 01-1029, December 20, 2001 (addition of certain did nothing more than make express what had been implicit in the claim as originally worded).

2. Rejection under 35 U.S.C. § 103(a)

Claims 29-35 stand rejected as being obvious over Babbitt *et al.* (U.S. Patent No. 5,766,920). In light of the Declaration of Dr. Triozzi submitted herewith, along with the previously submitted arguments and Appeal Brief, Applicants respectfully traverse the rejections of the claims and grounds therefor.

As an initial point, Applicants draw the Examiner's attention to the instant application's filing date (claiming priority to February 21, 1996), which has priority over Babbitt *et al.* (issued June 16, 1998). The examiner has provided no basis under which an earlier priority date should be afforded to Babbitt *et al.* Therefore, Babbitt *et al.* is ineligible as a reference to be cited against the claims under examination.

Nonetheless, even if Babbitt *et al.* were a valid reference, Applicants submit that the invention taught by Babbitt *et al.* does not render obvious the expansion of activated T-helper cells derived from lymph nodes. Babbitt *et al.* teach use of peripheral blood as a preferred source of T-helper cells, and uses repetitive rounds of a multi-step procedure to co-stimulate the low numbers of T-helper cells in peripheral blood. Applicants note that the amended claims do not claim use of peripheral blood lymphocytes as a source of mononuclear cells for the *in vitro* cell manipulation. Applicants actually teach away from using peripheral blood lymphocytes as a source of T-helper cells, because peripheral blood is ineffective to serve as a source of T-cells when used in the method taught in by the invention. The procedure disclosed by Applicants, contrary to that of Babbitt *et al.*, maintains the viability of antigen presenting cells present in lymph nodes. The present invention differs so substantially from that disclosed by Babbitt *et al.*, and offers such substantial improvements in ease of application and reliability that the applicant's invention is not obvious in light of Babbitt *et al.*

Applicants teach use of excised lymph node tissue as a source of immune cells because this cell source offers numerous advantages over peripheral blood as a cell source. Lymph nodes are enriched in antigen presenting cells, particularly dendritic cells, which are at low concentrations in peripheral blood.

3. The Triozzi Affidavit demonstrates that the Invention is New and Not Obvious.

Dr. Pierre L. Triozzi supervised a pilot study implementing an embodiment of the present invention disclosed in a related application. The Examiner is invited to carefully read the enclosed affidavit of Dr. Triozzi, which was previously submitted in prosecution of U.S. Application Ser. No. 08/943,993, to which priority has been claimed. Initially, it will be observed that Dr. Triozzi is eminently qualified as an expert in this field. Dr. Triozzi reports the results of experiments testing the cell expansion of CD4⁺ and CD8⁺ cells derived from peripheral blood and from excised lymph nodes.

The experimental results reported by Triozzi clearly show that CD4⁺ and CD8⁺ cells were expanded to a far lesser degree when the cell line progenitors were derived from peripheral blood than when derived from lymph nodes. Next, Dr. Triozzi reports the results of cytokine production assays (MIP-1 and RANTES) from cells expanded from lymph node lymphocytes and from peripheral blood lymphocytes. Again, the amount of cytokine produced from the cells expanded from lymph node lymphocytes was substantially greater than from cells expanded from peripheral blood.

These tests demonstrate that lymphocytes derived from different sources do not possess equivalent generative potential. The source of lymphocytes surely impacts their use in adoptive cellular therapy. It is not surprising that prior workers in this field using peripheral blood lymphocytes for adoptive cellular therapy could not effectively treat HIV infection. Thus, it is not obvious that lymph nodes are a preferred source of lymphocytes for cell expansion and that peripheral blood lymphocytes lack equivalent generative potential.

Though Babbitt's disclosure suggests in passing that lymph nodes could be used as a source of lymphocytes, lymph nodes are not a preferred source. Indeed, there is no way to predict from the experimental results reported by Babbitt that lymph node lymphocytes would be a preferred or even an enabling source for basing an adoptive cellular therapeutic in the treatment of HIV patients. This is especially telling in view of the excellent scientific data, including patient data, presented in the above-identified application. As Dr. Triozzi states, "If anything, it may be considered counter-intuitive to

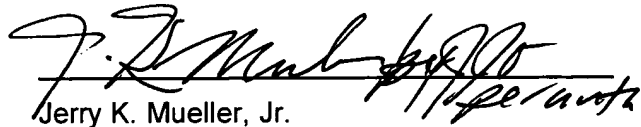
use a major reservoir of HIV, *i.e.*, lymph nodes, and the central target of HIV infection, *i.e.*, activated CD4⁺ cells, in the adoptive cellular therapy of HIV infection." ¶ 14 of Dr. Triozzi's December 18, 1997 affidavit. This statement of Dr. Triozzi is not controverted by any reference or combination of references.

The present invention demonstrates both surprising and unexpected efficacy from making an educated choice among the many potential sources of lymphocytes. Thus, Babbitt *et al.* fails to render obvious the present invention. Applicants' remarks, taken together with the Affidavit of Dr. Triozzi, overcome these grounds of rejection.

Accordingly, in view of the amendments, affidavit, and remarks submitted herewith, allowance of all claims and passage to issue of this application respectfully is requested. Should any questions remain, the Examiner respectfully is invited to telephone the undersigned.

Respectfully submitted,

Date: 12/14/05

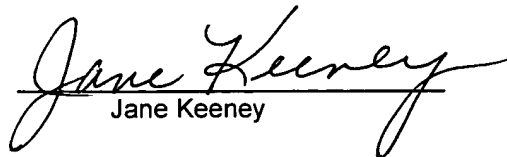

Jerry K. Mueller, Jr.

Reg. No. 27,576
MUELLER AND SMITH, L.P.A.
MUELLER-SMITH BUILDING
7700 Rivers Edge Drive
Columbus, Ohio 43235-1355
Tel.: 614-436-0600
Fax: 614-436-0057
email: smueller@muellersmith.com

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited on December 14, 2005 with the United States Postal Service as first class mail in an envelope addressed to:

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450


Jane Keeney